Diagnostic test accuracy of informant based tools to diagnose dementia in older hospital patients with delirium

Jackson, Thomas; MacLullich, Alasdair MJ; Gladman, J; Lord, Janet; Sheehan, Bart

DOI:
10.1093/ageing/afw065
10.1093/ageing/afw065

Document Version
Peer reviewed version

Citation for published version (Harvard):
Jackson, T, MacLullich, AMJ, Gladman, J, Lord, J & Sheehan, B 2016, 'Diagnostic test accuracy of informant based tools to diagnose dementia in older hospital patients with delirium: a prospective cohort study', *Age and Ageing*, vol. 45, no. 4, pp. 505-511. https://doi.org/10.1093/ageing/afw065, https://doi.org/10.1093/ageing/afw065

Diagnostic test accuracy of informant based tools to diagnose dementia in older hospital patients with delirium: A prospective cohort study

Abstract

Background: Delirium and dementia co-exist commonly in hospital. Older people with delirium have high rates of undiagnosed dementia, but delirium affects the use of cognitive testing in dementia diagnosis. Novel methods to detect dementia in delirium are needed. The purpose of the study was to investigate the diagnostic test accuracy of informant tools to detect dementia in hospitalised older people with delirium.

Methods: The presence of dementia on admission was assessed using the short form of the Informant Questionnaire of Cognitive decline in the Elderly (IQCODE-SF) and Alzheimer's Disease 8 (AD8) in people over 70 years old with delirium. Reference standard diagnosis was made using Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV) criteria at three months. The main outcome measures were the diagnostic test accuracy of the IQCODE-SF and the AD8 in diagnosing DSM-IV dementia.

Results: Dementia prevalence at 3 months was 61%. The area under the receiver operating characteristic curve (AUROC) was 0.93 ($p<0.0005$) for admission IQCODE-SF and 0.91 ($p<0.0005$) for admission AD8. An IQCODE-SF test result of >3.82 on admission had a sensitivity of 0.91 (0.79-0.97) and specificity of 0.93 (0.76-0.99) for detecting dementia. An AD8 of >6 had a sensitivity of 0.83 (0.69-0.92) and specificity of 0.90 (0.72-0.97) for detecting dementia.

Conclusion: The IQCODE-SF and AD8 are sensitive and specific tools to detect prior dementia in older people with delirium. The routine use of either tool in practice could have important clinical impact, by improving the recognition and hence management of those with dementia.

Introduction

Dementia is a chronic neurodegenerative disease characterised by progressive cognitive decline, amnesic deficits and functional deficits [1]. Dementia is common among older hospital patients. In acute medical admissions cognitive impairment affects 50% [2] and dementia up to 42% [3, 4]. Older patients with dementia have higher rates of adverse events in hospital [5] as well as higher mortality and institutionalisation [6]. However, dementia in this population is under-recognised, with up to a half of older patients in hospital with dementia not having a recognised diagnosis [3].

Delirium is a severe neuropsychiatric syndrome characterised by an acute change in cognition, attentional deficits and altered arousal [7]. Delirium is also common in older hospital inpatients, affecting 15-25% of acute admissions [2, 8]. Apart from age, cognitive impairment is the most important risk factor for delirium [9]. Therefore, older patients with delirium are a key target population to improve identification of dementia within the general hospital.

Few traditional performance based assessments (cognitive tests) for dementia have been validated in the general hospital and they are not valid in the context of patients with delirium [10]. As delirium, by definition, is associated with an acute cognitive change from baseline, novel strategies to identify dementia in delirium are required. Brief informant based screening tools with relatives and carers are thoroughly validated for community use [11] but have only been validated in a single study in hospital inpatients [12] and not in those with delirium.

The report aimed to assess the diagnostic test accuracy of two informant tools to detect prior dementia in older patients with current delirium.

Methods

Recruitment

Patients aged 70 years and over with an unplanned medical admission to a United Kingdom university hospital between March 2013 and November 2014 were screened for delirium. The screening used the Confusion Assessment Method (CAM) [13], Abbreviated Mental Test Score (AMTS) [14], the Digit Span test, and a detailed review of the medical notes. An expert geriatrician (TAJ) completed all screening. If participants met the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV-TR) criteria for delirium [15] they were eligible for the study. Potential participants who were unable to communicate because of severe sensory impairment or inability to speak in English were excluded, as were those deemed to be at risk of imminent death.

Patients with delirium were then invited to participate. Informed consent was sought from the potential participant if they had capacity. For those who lacked capacity to give informed consent, the next of kin was consulted in accordance with the provisions of the Mental Capacity Act with respect to participation in research, and they were also approached to act themselves as informants in the study. Informed consent was then gained from the informants.

An informant interview enquired about previous diagnosis of dementia or cognitive impairment. The informant was then asked to complete two rating scales in order. First the short form of the Informant Questionnaire of Cognitive Decline in the Elderly (IQCODE-SF)[16] and second, the ‘AD8: The Washington University Dementia Screening Test’, also

referred to as the Eight-item Interview to Differentiate Aging and Dementia (AD8) [17]. These were chosen as they are freely available and have face validity. After explanation of the tests, they were then completed in private and placed in an envelope to ensure appropriate blinding.

Informant tools

The IQCODE-SF asks the informant to rate changes in cognition, memory and behaviours over a 10-year period. It has been validated in both primary care settings [11], community settings [18] and secondary care settings [19] to diagnose dementia. It takes about 10 minutes to complete. The scale consists of 16 items rated one to five where higher scores indicate a greater degree of cognitive impairment, from which a mean is derived (also ranging from one to five). In instances where ratings were missing for an item, a mean score was calculated from the items that were completed. The introductory wording was changed to 'Now we want you to remember what your friend or relative was like 10 years ago and to compare it with what he/she was like *before they got the illness that brought them to hospital'*.

The AD8 is a shorter screening informant interview, asking the informant to rate memory and thinking changes over a few years, rating eight items either yes, no or don't know. It takes five minutes to complete and has been found to be sensitive and specific to dementia in a memory clinic population [65]. The test is scored from zero to a maximum of eight, where higher scores indicate a greater degree of cognitive impairment. Missing values were assumed to be 'don't know', so scored as zero.

Reference Standard

At 3 months an assessment in survivors was undertaken to determine a reference diagnosis of dementia at the time of index admission. The assessment was carried out by TAJ at the patient's own home or hospital if they were still an inpatient. The assessment was carried out blinded to the results of the IQCODE-SF and AD8. It is not possible to diagnose DSM-IV dementia in the presence of delirium so follow-up at three months was chosen as the best balance to allow recovery from delirium and ensuring an accurate diagnosis of dementia at the index admission. The presence of persistent delirium was first assessed for using DSM-IV-TR criteria. If no delirium was present a standardised history and examination, including the Addenbrooke's Cognitive Examination III (ACEIII) [20], was performed to establish the presence or absence of dementia at the time of index admission (before the onset of the delirium). Dementia and subtype was diagnosed using the DSM-IV criteria[21]: (1) the development of multiple cognitive deficits, including memory impairment, and (2) the impairment is sufficiently severe to cause impairment in occupational or social function. To make the diagnosis of dementia at the index admission the symptoms of cognitive decline had to have been present for at least 6 months prior to the admission with delirium.

Statistical analysis

Receiver operating characteristic curves were generated for both tests and a calculation of the area under the curve (AUROC) made. Sensitivity, specificity, the positive likelihood ratio (LR+), and the negative likelihood ratio (LR-) were calculated from the best cut-offs. In evaluating the relative misclassification costs in this population we selected cut-offs that minimized false positive diagnoses, reducing the burden of potentially stressful and unnecessary further investigation. Data were analysed using IBM SPSS version 20 for Windows.

Please see Appendix 1 in the supplementary data on the journal website (http://www.ageing.oxfordjournals.org/) for details of the power calculations.

All assessments were carried out by a single trained assessor (TAJ). The protocol was assessed and approved by the Bradford Ethics Committee, part of the Yorkshire and Humber National research and Ethics Service (Ref: 12/YH/0534). The study was reported using the Standards for Reporting of Diagnostic Accuracy (STARD) statement with specific reference to studies of diagnostic test accuracy in dementia [22, 23] (Check list and flow chart available in Appendix 2 in the supplementary data)

Results

Delirium was diagnosed in 228 (17.2%) of 1327 older people screened for delirium. 125 of this group of 228 (54.8%) were recruited. The main reason for non-recruitment was the lack of an available consultee or informant (57/228, 25%). 22/228 (10%) were deemed at risk of imminent death, 15/228 (7%) were not able to communicate in English, the consultee declined participation in 2/228 (1%) and 7/228 (3%) had been previously recruited.

Of the 125 recruited, 77 (62%) had a full assessment for the reference standard diagnosis. 25/125 (20%) had died, 10/125 (8%) declined the follow-up visit, 8/125 (6%) were not contactable for an assessment, and 5/125 (4%) had persistent delirium at assessment. There was no difference in age, gender or admission dementia status between those assessed for dementia at 3 months and those not. The mean age of the final sample assessed for reference criterion diagnosis of dementia was 84.4 and 69% were female. Participant flow through the study is illustrated in figure 1.

At three month assessment 47/77 (61%) were diagnosed with dementia, 14/77 (18%) were diagnosed with MCI, and 16/77 (21%) had no cognitive impairment. Of those with dementia, this was newly diagnosed in 17/47 (36%).

In diagnosing DSM-IV dementia the AUROC curve for the admission IQCODE-SF was 0.93 (95% CI 0.86-1.00, $p<0.0005$) and for the admission AD8 it was 0.91 (95% CI 0.83-0.98, $p<0.0005$). There was no statistical difference between the AUROC curves ($z=0.45$, $p=0.65$) [24]. The selected cut off of >3.82 for the IQCODE-SF gave a sensitivity of 0.91, a specificity of 0.93, LR+ of 13.72 and a LR- of 0.09. The selected cut off of >6 for the AD8 gave a sensitivity of 0.83, a specificity of 0.90, a LR+ of 8.30 and a LR- of 0.19.

The traditional cut off of the IQCODE-SF for diagnosing dementia in the general hospital [25] is ≥3.44. Using this cut off gave a greater sensitivity of 0.98 at the expense of a lower specificity of 0.67.

Table 1 illustrates the diagnostic test accuracy values for the IQCODE-SF and AD8 including confidence intervals at various cut-offs. Please see Figure 1 in the supplementary data on the journal website http://www.ageing.oxfordjournals.org/ for the ROC curves for the IQCODE-SF and AD8.

Discussion

The main new finding in this study is that we found excellent diagnostic test accuracy of the IQCODE-SF and AD8 in diagnosing dementia in older people presenting with delirium.

Specifically, we found that the IQCODE-SF and AD8 had excellent sensitivity, specificity and discriminatory ability. An AUROC of greater than 0.9 is considered excellent. Based on the findings from this study, taking 100 older people with delirium, IQCODE-SF at a cut off of >3.82 would correctly identify 56 of the 61 with dementia and would falsely imply a diagnosis of dementia in 3 of the 39 without dementia. Interpreting the likelihood ratios of the IQCODE-SF at a cut off of >3.82 to diagnose dementia, a positive test is 13 times more likely to occur in someone with dementia rather than someone without dementia. A negative test is 0.07 times less likely to occur in someone with dementia rather than someone without. This indicates good discrimination after a test has been performed. A positive likelihood ratio of greater than 10 and a negative likelihood ratio of less than 0.1 indicates a test is useful [26].

Neither the IQCODE-SF nor the AD8 have previously been validated to diagnose dementia in patients with delirium. One previous study has examined the diagnostic test accuracy of the IQCODE-SF to diagnose dementia in older hospital inpatients, excluding those with delirium. This reported a sensitivity of 1.00 and specificity of 0.86 for detecting DSM-IIIR dementia at a cut-off of >3.44 [12]. They report at ≥3.76 cut off a sensitivity of 0.92 and specificity of 0.93 for the IQCODE-SF, which are very similar to our reported values. It is also worth noting that the prevalence of dementia was much lower (10%) in this study. Although the IQCODE-SF has not been formally assessed in people with delirium, it is commonly used as a proxy for previous cognitive impairment in delirium research using different cut offs. A cut off of >3.5 has been used in a general hospital population [27] and our findings suggest these cut offs may be too low.

Although both tests have similar diagnostic accuracy both have advantages and disadvantages. The AD8 is simpler and quicker to complete, however it has a higher number

of false positives. The IQCODE-SF still only takes a maximum of 10 minutes to complete and the extra detail gathered may be of clinical relevance. The IQCODE-SF has been translated into 14 languages. Both are freely available without cost [28, 29]. On balance we would recommend using the IQCODE-SF at a cut off of >3.82 to detect dementia.

The study has important strengths and limitations. The reported prevalence of delirium of 17.9% is similar to previous studies in acute admissions [8] indicating the screening was robust. We recognise the difficulty in diagnosing dementia among patients in hospital with delirium, so strict reference criteria were applied by an experienced and trained specialist assessor. The assessor was blinded to the index test result. We accept that the diagnosis of dementia before the hospital admission with delirium could be affected by recall bias, and the presence of post-delirium cognitive impairment. However, the assessor aimed to take this into account when conducting his assessment. The diagnosis of prior cognitive impairment did not rely exclusively on cognitive testing at three months, but also on the clinical history. Therefore, we believe the findings to be robust and are representative of a real world general hospital. The study recruited to the appropriately powered sample size. The study did not recruit all patients diagnosed with delirium, the main reason being the lack of an available consultee and/or informant. However, there were no gender or age differences between those recruited and those not. Not all participants were available for reference diagnosis assessment at 3 months. The main reason was mortality, with 25 (20%) having died prior follow-up. This is in keeping with the expected mortality of delirium [27] and importantly higher mortality would be expected in those with dementia.

The other factor that could reduce the generalisability of our findings is the non-availability of an informant In our study one-quarter (57/228) of patients with delirium had no informant available, so this may affect the utility of informant tools in practice. However, the

recruitment of an informant in our study was time limited so we feel in real world practice this proportion would be lower. There was no difference in age and gender between the recruited and non-recruited groups. The informant information may also be affected by recall bias as characteristics of the informant may influence the result such as depression or cognitive impairment. However the strength of an informant tools is that it to some extent mitigates problems with pre-existing educational background, culture or language difficulties.

The significance of our findings to the research community is that the IQCODE-SF or AD8 at validated cut offs can now be used to robustly identify prior dementia in studies of delirium cohorts in general hospital.

Our findings could impact significantly on clinical practice, given the high prevalence of delirium and unrecognised dementia in the general hospital. Figure 2 is a flow chart extrapolating our diagnostic and prevalence data to a hypothetical acute hospital with 1000 beds. Although we acknowledge there are differing views, a timely diagnosis of dementia during hospital admission may ameliorate adverse events associated with a hospital stay [5], allow signposting to a suitable cohort ward [30] or a trigger the need for comprehensive geriatric assessment [31]. It could also lead to extra care in communication with patients, especially around issues of capacity assessment and consenting for interventions.

Conclusions

Both the IQCODE-SF and AD8 are sensitive and specific tools to detect dementia in older people presenting to hospital with delirium. They are simple and quick to administer as well as being freely available. Given the high prevalence of delirium in older people in hospital

the routine use of either tool in practice will have important clinical impact, potentially improving the formal recognition of dementia as well as having immediate implications for the inpatient care of this vulnerable population.

Competing Interests

The authors declare that they have no competing interests

Declaration of sources of funding

TAJ was supported jointly by the Research into Ageing Fund; a fund set up and managed by Age UK and the British Geriatrics Society (#367). The study sponsor had no role in either study design; the collection, analysis, and interpretation of data; the writing of the report; and in the decision to submit the paper for publication

Acknowledgements

We gratefully acknowledge the participants, carers and consultees who took part in the study. We gratefully acknowledge Dr Jenni Harrison of the University of Leicester for her help with statistical analysis.

References

1. Bayer A. Chapter 52 - Presentation and Clinical Management of Dementia. In: Woodhouse HMFR, editor. Brocklehurst's Textbook of Geriatric Medicine and Gerontology (seventh Edition). Philadelphia: W.B. Saunders; 2010. p. 392-401.

2. Goldberg SE, Whittamore KH, Harwood RH, Bradshaw LE, Gladman JR, Jones RG, et al. The prevalence of mental health problems among older adults admitted as an emergency to a general hospital. Age Ageing. 2012 Jan;41(1):80-6.

3. Sampson EL, Blanchard MR, Jones L, Tookman A, King M. Dementia in the acute hospital: prospective cohort study of prevalence and mortality. Br J Psychiatry. 2009 Jul;195(1):61-6.

4. Timmons S, Manning E, Barrett A, Brady NM, Browne V, O'Shea E, et al. Dementia in older people admitted to hospital: a regional multi-hospital observational study of prevalence, associations and case recognition. Age Ageing. 2015 November 1, 2015;44(6):993-9.

5. Mecocci P, von Strauss E, Cherubini A, Ercolani S, Mariani E, Senin U, et al. Cognitive impairment is the major risk factor for development of geriatric syndromes during hospitalization: results from the GIFA study. Dement Geriatr Cogn Disord. 2005;20(4):262-9.

6. Sampson EL, Leurent B, Blanchard MR, Jones L, King M. Survival of people with dementia after unplanned acute hospital admission: a prospective cohort study. Int J Geriatr Psychiatry. 2013 Oct;28(10):1015-22.

7. Inouye SK, Westendorp RGJ, Saczynski JS. Delirium in elderly people. The Lancet. 2014;383(9920):911-22.

8. Collins N, Blanchard MR, Tookman A, Sampson EL. Detection of delirium in the acute hospital. Age Ageing. 2010 Jan;39(1):131-5.

9. Ahmed S, Leurent B, Sampson EL. Risk factors for incident delirium among older people in acute hospital medical units: a systematic review and meta-analysis. Age Ageing. 2014 May;43(3):326-33.

10. Jackson TA, Naqvi SH, Sheehan B. Screening for dementia in general hospital inpatients: a systematic review and meta-analysis of available instruments. Age Ageing. 2013 Nov;42(6):689-95.

11. Harrison JK, Fearon P, Noel-Storr AH, McShane R, Stott DJ, Quinn TJ. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the diagnosis of dementia within a general practice (primary care) setting. The Cochrane database of systematic reviews. 2014;7:CD010771.

12. Harwood DM, Hope T, Jacoby R. Cognitive impairment in medical inpatients. I: Screening for dementia--is history better than mental state? Age Ageing. 1997 Jan;26(1):31-5.

13. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann Intern Med. 1990 Dec 15;113(12):941-8.

14. Hodkinson HM. Evaluation of a mental test score for assessment of mental impairment in the elderly. Age Ageing. 1972 Nov;1(4):233-8.

15. American Psychiatric Association. Diagnostic and statistical manual of mental disorders : DSM-IV-TR. Washington, DC: American Psychiatric Association; 2000.

16. Jorm AF. A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): development and cross-validation. Psychol Med. 1994 Feb;24(1):145-53.

17. Galvin JE, Roe CM, Powlishta KK, Coats MA, Muich SJ, Grant E, et al. The AD8: a brief informant interview to detect dementia. Neurology. 2005 Aug 23;65(4):559-64.

18. Quinn TJ, Fearon P, Noel-Storr AH, Young C, McShane R, Stott DJ. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the diagnosis of dementia within community dwelling populations. The Cochrane database of systematic reviews. 2014;4:CD010079.

19. Harrison JK, Fearon P, Noel-Storr AH, McShane R, Stott DJ, Quinn TJ. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the diagnosis of dementia within a secondary care setting. The Cochrane database of systematic reviews. 2015 Mar 10;3:CD010772.

20. Hsieh S, Schubert S, Hoon C, Mioshi E, Hodges JR. Validation of the Addenbrooke's Cognitive Examination III in frontotemporal dementia and Alzheimer's disease. Dement Geriatr Cogn Disord. 2013;36(3-4):242-50.

21. American Psychiatric Association. Diagnostic and statistical manual of mental disorders : DSM-IV. Washington, DC: American Psychiatric Association; 1994.

22. Noel-Storr AH, McCleery JM, Richard E, Ritchie CW, Flicker L, Cullum SJ, et al. Reporting standards for studies of diagnostic test accuracy in dementia: The STARDdem Initiative. Neurology. 2014 Jul 22;83(4):364-73.

23. Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al. The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. Ann Intern Med. 2003 Jan 7;138(1):W1-12.

24. Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology. 1983 Sep;148(3):839-43.

25. British Geriatric Society. Delirious about Dementia: Towards better services for patients with cognitive impairment by geriatricians. London2005.

26. Jaeschke R, Guyatt G, Lijmer J. Diagnostic tests. Users' guides to the medical literature. Chicago: AMA Press; 2002. p. 121-40.

27. O'Regan NA, Ryan DJ, Boland E, Connolly W, McGlade C, Leonard M, et al. Attention! A good bedside test for delirium? J Neurol Neurosurg Psychiatry. 2014 Oct;85(10):1122-31.

28. Australian National University. Informant questionnaire on cognitive decline in the elderly. 2015 [17/03/2015]; Available from: http://crahw.anu.edu.au/risk-assessment-tools/informant-questionnaire-cognitive-decline-elderly.

29. Knight Alzheimer's Disease Research Centre. AD8 Permission Policy. 2015 [17/03/2015]; Available from: http://knightadrc.wustl.edu/About_Us/AD8_Permission.htm.

30. Goldberg SE, Bradshaw LE, Kearney FC, Russell C, Whittamore KH, Foster PE, et al. Care in specialist medical and mental health unit compared with standard care for older people with cognitive impairment admitted to general hospital: randomised controlled trial (NIHR TEAM trial). BMJ. 2013;347:f4132.

31. Ellis G, Whitehead MA, Robinson D, O'Neill D, Langhorne P. Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomised controlled trials. BMJ. 2011;343:d6553.

Table 1: Diagnostic test accuracy of the IQCODE-SF and AD8 at different cut-offs to diagnose dementia. Sens=sensitivity, Spec=specificity, LR+ = positive likelihood ratio, LR- = negative likelihood ratio, AUROC=area under the receiver operating characteristic curve. 95% confidence intervals in brackets after all values.

	Test/ cut off	Sens	Spec	LR+	LR-	AUROC
Against diagnosis of dementia	IQCODE ≥3.44	0.98 (0.87-0.99)	0.67 (0.47-0.82)	2.94 (1.77-4.88)	0.03 (0.01-0.23)	0.93 (0.86-1.00, p<0.0005)
	IQCODE >3.82	0.91 (0.79-0.97)	0.93 (0.76-0.99)	13.72 (3.58-52.50)	0.09 (0.04-0.23)	
Prevalence 61%	AD8 >2	0.97 (0.87-0.99)	0.40 (0.23-0.60)	1.63 (1.21-2.19)	0.05 (0.01-0.41)	0.91 (0.83-0.98, P<0.0005)
	AD8 >6	0.83 (0.69-0.92)	0.90 (0.72-0.97)	8.30 (2.81-24.47)	0.19 (0.09-0.36)	

Figure 1:

Flowchart of recruitment through study with demographics of recruited participants. ♀ = female

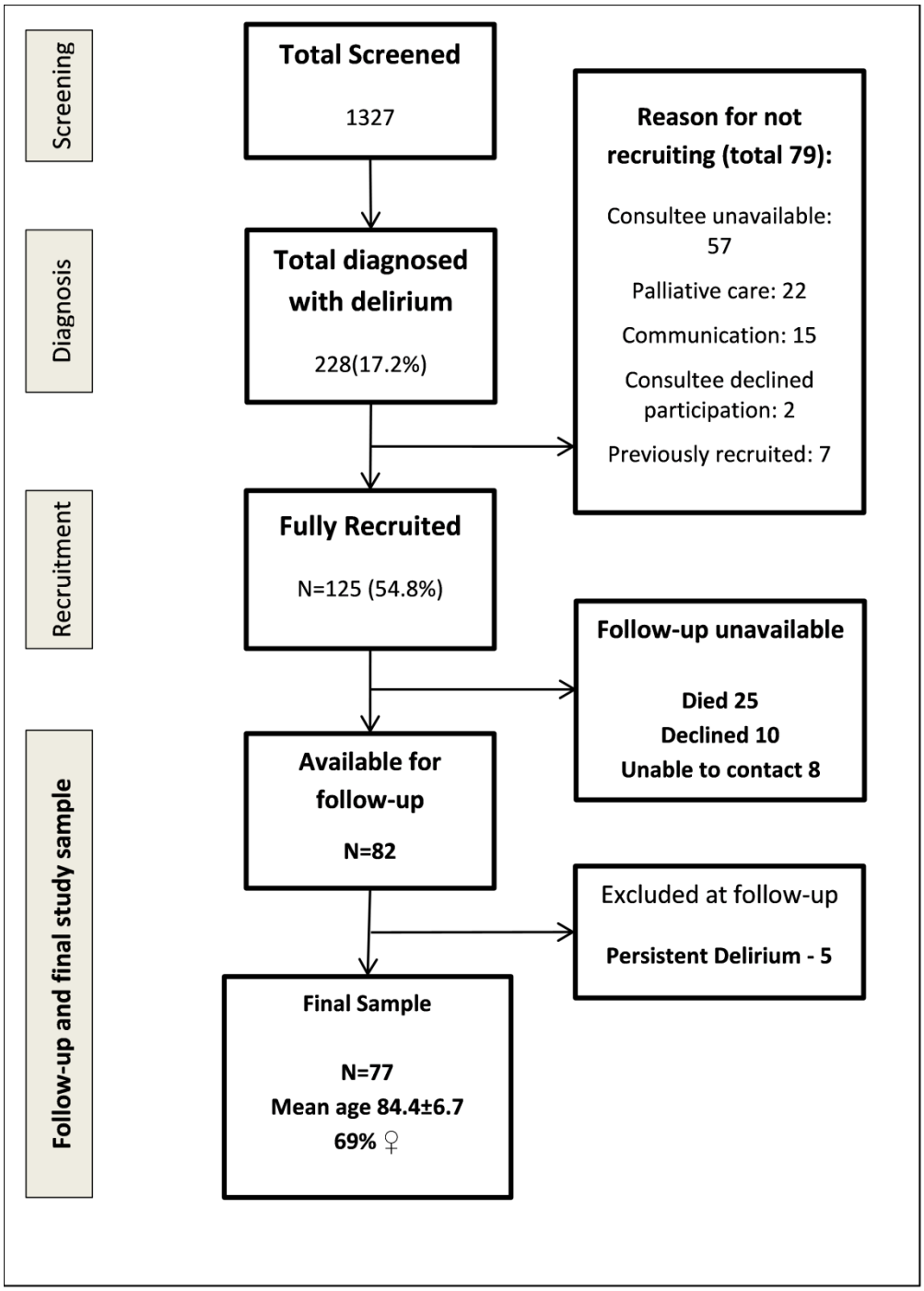
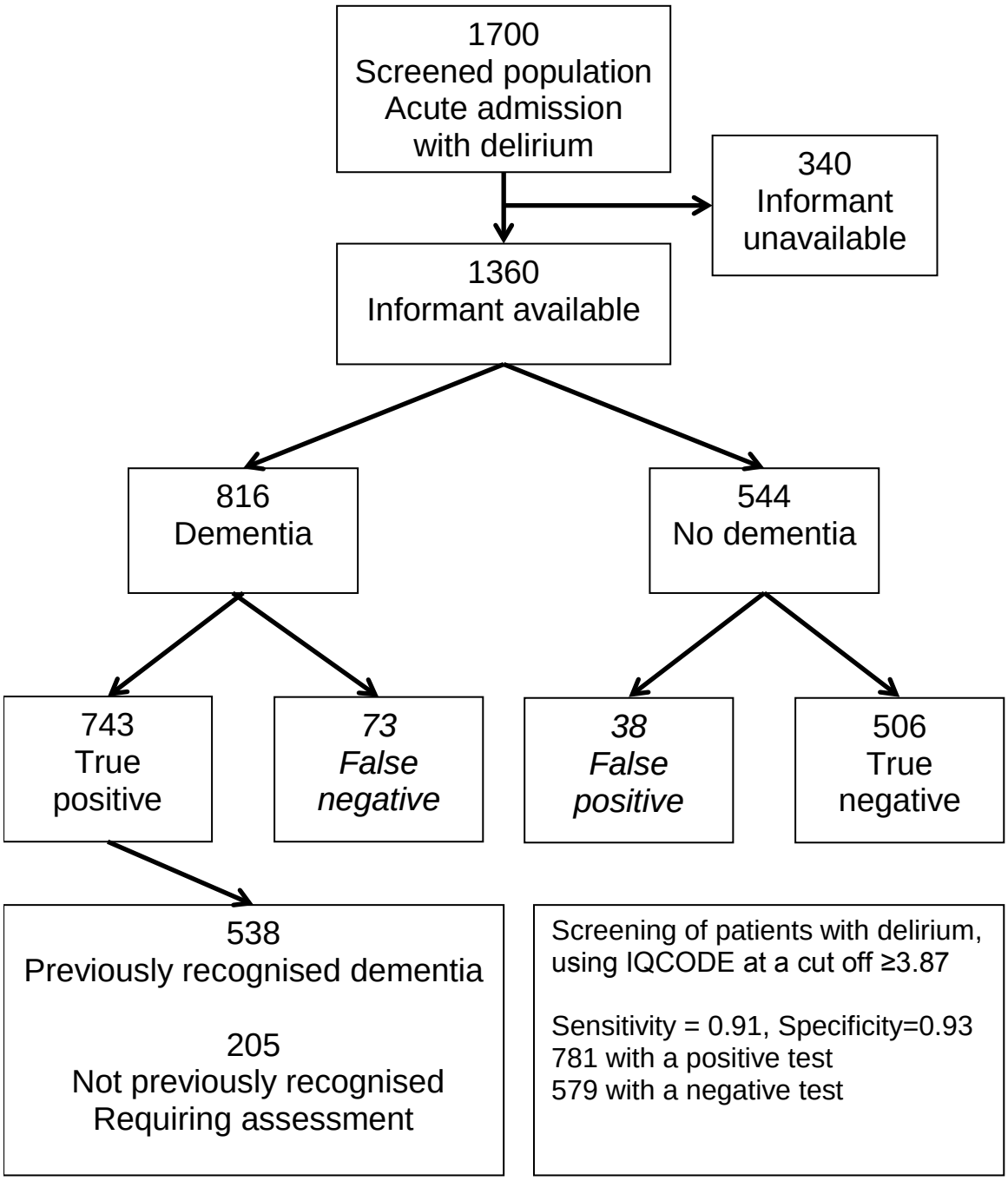


Figure 2:

Flow chart illustrating the use of the IQCODE-SF for screening patients with delirium for dementia in a hypothetical 1,000 bedded hospital and 10,000 non-elective admissions of older people yearly. We expect 1700 (17 %) would have delirium, with 60% of those also having dementia. 33% of that dementia will be unrecognised. We would expect 20% of patients to have no informant available.


1700
Screened population
Acute admission
with delirium
340
Informant
unavailable
1360
Informant available
816
Dementia
544
No dementia
743
True
positive
73
False
negative
38
False
positive
506
True
negative
538
Previously recognised dementia
205
Not previously recognised
Requiring assessment
Screening of patients with delirium, using IQCODE at a cut off ≥3.87
Sensitivity = 0.91, Specificity=0.93
781 with a positive test
579 with a negative test